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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/073,596	05/06/1998	RALPH M. STEINMAN	20164000US5	9977

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/073,596	STEINMAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82,84-96 and 98-121* is/are pending in the application.

4a) Of the above claim(s) *82,84-88,90,93,96,98,100 and 102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89, 91, 92, 94, 95, 99, 101, 103-121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 7/08/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 7/08/05, have been entered.

2. Claims 82, 84-88, 90, 93, 96, 98, 100, and 102 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Note regarding Claim 96, in the claims filed 4/12/02 the claim recited a composition comprising an enriched and expanded population dendritic cell (DC) precursors. In the claims filed 10/30/03 the claim recited a composition comprising an enriched and expanded population of human DCs. As the claim does not appear to have been amended, it stands withdrawn as reading on an enriched and expanded population DC precursors.

Regarding Claim 84, it is unclear whether this claim reads on antigen-activated DC or DC precursors. It is clear, however, that dependent Claims 85-88 recite DC precursors. Accordingly, Claim 84 is considered to also read on DC precursors and is therefore withdrawn from consideration.

Claims 89, 91-92, 94-95, 99, 101, 103-120, and newly added Claim 121, are being acted upon.

3. In view of Applicant's amendments and remarks, filed 7/08/05, the previous rejections of Claim 109 and 115 under the first paragraph of 35 U.S.C. 112 for the introduction of new matter have been withdrawn. Additionally, the rejections of Claims 89, 91-92, 94-95, 99, 101, 103-120 for the recitation of, "A composition comprising an enriched and expanded population of antigen-activated dendritic cells" and "a modified antigen", have also been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 110, 118, and 119 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record. This is a new matter rejection.

As set forth previously, the specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) the recitation in Claim 110 of, "wherein the cell aggregates are subcultured about every 3 to 30 days."

B) the recitation in Claims 118 and 119 of, "wherein the dendritic cell precursors are cultured in the presence of antigen."

Applicant arguments, filed 7/08/05, have been fully considered but are not found persuasive.

Applicant argues that support for A) can be found in original Claim 14.

A review of the original claims shows that the claimed limitation was further limited, i.e., "one to five times every 3 to 30 days".

Regarding B) Applicant cites original Claim 65, and pages 10 and 12 of the specification.

A review of the original claims and specification shows no support for the time limitations of the claims, i.e., "1-48 hours" (Claim 118) and "about 20 hours" (Claim 119).

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple

assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 89, 91-92, 94-95, 99, 101, 103-120, and newly added Claim 121, stand/are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 45 and 46 of copending Application No. 10/287,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass antigen-activated dendritic cells.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant again requests that this rejection be held in abeyance until the finding of allowable subject matter.

8. The following are new grounds for rejection.

9. Claims 89, 91-92, 94-95, 99, 101, 103-120, and newly added Claim 121 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) An *in vitro* composition comprising antigen-activated dendritic cells presenting fragmented antigen derived from an *in*

vitro culture of an enriched and expanded population of proliferating dendritic cell precursors by a method comprising:

providing a tissue source comprising dendritic cell precursors;

optionally treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors;

culturing the tissue source on a substrate in a culture medium comprising GM-CSF to obtain cell clusters;

subculturing the cell clusters to produce cell aggregates comprising proliferating dendritic cell precursors; and

subculturing the cell aggregates at least one time to enrich the proportion of dendritic cell precursors;

wherein the dendritic cell precursors are cultured *in vitro* in the presence of an antigen for time sufficient to allow the antigen to be fragmented and presented (Claim 101).

B) An *in vitro* composition comprising antigen-activated dendritic cells presenting fragmented antigen derived from an *in vitro* culture of population of enriched and expanded proliferating dendritic cell precursors which were contacted in vitro with an antigen in the presence of GM-CSF for a sufficient time for antigen fragmentation and presentation to occur (Claim 120).

It is noted that no support for the limitations of these claims as they are now recited has been submitted. Limitations have been added amendment by amendment such that the claimed invention has evolved into one that is not supported by the specification. In particular, note that the method of Claim 101 is in general disclosed by the specification as a method of deriving mature DCs, not the antigen-activated DCs of the claims. Also note that not all the steps of the claimed method are precisely those set forth in the specification, for example, the "optional" step of treating the tissue source comprising dendritic cell precursors to increase the proportion of dendritic cell precursors does not appear to be optional in the specification.

And additionally note that it is not even clear how the claimed invention actually evolved. For example, the "enriched and expanded population of processed antigen presenting dendritic cell precursors" of Claim 101 as set forth in the submission of 7/09/01 evolved into the "population of antigen-activated dendritic cell precursors" of 4/12/02, apparently

without amendment.

Applicant's citing of support for each of the limitations of the instant claims, in their instant context, would be of significant help in expediting prosecution.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 89, 91-92, 94-95, 99, 101, 103-120, and newly added Claim 121, are rejected under 35 U.S.C. 103(a) as being unpatentable over Sornasse et al. (1992, IDS) in view of Aldovini et al. (1991, of record).

Sornasse et al. teaches a pharmaceuticals composition comprising DCs pulsed with polypeptide or peptide antigens (see particularly page 16, column 2) that process and present antigen (see particularly Figure 2).

The reference differs from the claimed invention in that it does not teach the use of a mycotuberculosis, specifically BCG, antigen.

Aldovini et al. teaches that BCG is a well-known mycobacterium antigen used in over two billion tuberculosis immunizations (as of 1991) (see particularly Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce antigen pulsed DCs that process and present antigen, as said pulsed DCs could be useful for immunization because of their natural adjuvant properties and because the dendritic cell would naturally select the antigen that could be presented on any particular MHC, as taught by Sornasse et al., substituting BCG as the antigen of choice, as taught by Aldovini et al. One of ordinary skill in the art at the time the invention was made would have been motivated to make said substitution because BCG is a well-known mycobacterium antigen used in over two billion

tuberculosis immunizations, as taught by Aldovini et al., to produce an improved pharmaceutical composition. Note that the references do not teach the dosage limitations of claims 99 and 103, however, the routine optimization of dosages falls well within the purview of one of ordinary skill in the art and thus lends no patentable weight to the claimed invention. Further note that the claims recite numerous limitations regarding the process by which the antigen-activated DCs of the instant claims are produced.

Regarding product-by-process claims, MPEP 2113 states:

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), and
"The Patent Office bears a lesser burden of proof in making out a case of *prima facie* obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983).

It is the Examiner's position that antigen-activated DCs of the instant claims are the DCs of the prior art.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina

Chan can be reached on (571) 272-0841.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

9/30/05

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